

Serial No. 09/156,367
Art Unit: 1645
Examiner: Marianne P. Allen

IN THE SPECIFICATION:

Please change the title of the invention to – A Method for Identifying
MLK Inhibitors for the Treatment of Neurological Conditions – .

IN THE CLAIMS:

Please cancel claims 26, and 33-43, without disclaimer or prejudice.

Please add the following claim:

44. The method of claim 9, wherein the neurotoxin is glutamate, quinolinic acid or kainic acid.

Please amend claims 1, 14, 19, 20, 21, 24, 25, 29, 30, and 32 as follows:

1. (Once Amended) A method for assessing a compound's ability to prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition, comprising:

a) contacting a compound with neuronal cells having activated MLK [and/or JNK] activity;

b) determining the number of neuronal cells that die;

wherein a decreased number of dead neuronal cells in the presence of the compound compared to the number of dead neuronal cells in the absence of the compound is indicative of the compound's ability to prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition.

14. (Once Amended) A method for assessing the ability of a [JNK and/or] MLK inhibitor to prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition, comprising:

- a) contacting a [JNK and/or] MLK inhibitor with neuronal cells having activated MLK [and/or JNK] activity;
- b) contacting, in the presence of the compound, surviving cells from step (a) with an agent that induces apoptosis; and
- c) comparing the level of apoptosis in the cell in the presence of the [JNK and/or] MLK inhibitor with the level of apoptosis in the cell in the absence of the [JNK and/or] MLK inhibitor;

wherein the [JNK and/or] MLK inhibitor is a potentially useful drug for treating the mammal when the level of apoptosis in the cell in the presence of the [JNK and/or] MLK inhibitor is less than the level of apoptosis in the cell in the absence of the [JNK and/or] MLK inhibitor.

19. (Once Amended) A method for screening a compound's ability to inhibit [JNK and/or] MLK activity and thereby prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition, comprising:

- a) contacting a compound with a [JNK and/or] MLK protein and substrate therefor;
- b) measuring the level of [JNK and/or] MLK activity;
- c) comparing the level of [JNK and/or] MLK activity in the presence of the compound with the level of [JNK and/or] MLK activity in the absence of the compound, wherein a decrease in [JNK and/or] MLK activity in the presence of the compound is indicative that the compound is a [JNK and/or] MLK inhibitor;

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d) contacting the compound with neuronal cells having activated MLK [and/or JNK] activity;

e) comparing the occurrence of apoptosis in the cell in the presence of the compound with the occurrence of apoptosis in the cell in the absence of the [JNK and/or] MLK inhibitor;

wherein the [JNK and/or] MLK inhibitor is a potentially useful drug for treating the mammal when the occurrence of apoptosis in the cell in the presence of the [JNK and/or] MLK inhibitor is less than the occurrence of apoptosis in the cell in the absence of the [JNK and/or] MLK inhibitor.

20. (Once Amended) The method of Claim 19, wherein [JNK is JNK1, JNK2 or JNK3 and] MLK is MLK1, MLK2 or MLK3, or combinations thereof.

21. (Once Amended) The method of Claim 20, wherein the [JNK and/or] MLK activity is kinase activity.

24. (Once Amended) A method for assessing a compound's ability to inhibit [JNK and/or] MLK activity and thereby prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition, comprising:

a) incubating a compound in the presence of [JNK and/or] MLK and appropriate [JNK and/or] MLK substrate therefor, under conditions sufficient for enzymatic activity; and

b) determining the presence or amount of phosphorylated product;

wherein a change in amount of phosphorylated product, when compared to incubating [JNK and/or] MLK with appropriate substrates absent the compound, is indicative of the compound's ability to inhibit the enzymatic activity of [JNK and/or] MLK and

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thereby prevent neuronal cell death in a mammal susceptible to or having a neurological condition.

25. (Once Amended) The method of Claim 24, wherein [JNK is JNK1, JNK2 or JNK3 and] MLK is MLK1, MLK2 or MLK3, or combinations thereof.

29. (Once Amended) A method for assessing a compound's ability to inhibit [JNK and/or] MLK kinase activity and thereby prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition, comprising:

a) contacting a neuronal cell with a compound under conditions sufficient for [JNK and/or] MLK enzymatic activity; and

b) determining the presence or amount of phosphorylated [JNK and/or] MLK product;

wherein a change in amount of phosphorylated product, when compared to incubating a cell absent the compound, is indicative of the compound's ability to inhibit [JNK and/or] MLK kinase activity and thereby prevent neuronal cell death occurring in a mammal susceptible to or having a neurological condition.

30. (Once Amended) The method of Claim 29 further comprising:

c) determining cell viability after step (a);

wherein any increase in the cell's viability status relative to a control is indicative of the compound's ability to inhibit [JNK and/or] MLK kinase activity thereby affecting the viability of the cell.

32. (Once Amended) The method of Claim 29, wherein [JNK is JNK1, JNK2 or JNK3 and] MLK is MLK1, MLK2 or MLK3, or combinations thereof.